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Coenzyme Q10 As A Risk Factor for Myofascial Pain Syndrome in Post-Ischemic Stroke Patients : A Literature Review

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ABSTRACT

Stroke remains a leading cause of long-term disability worldwide, with 85% of cases classified as ischemic due to arterial blockage and resulting neuronal injury. Among post-stroke complications, musculoskeletal disorders significantly impact quality of life and rehabilitation outcomes. Myofascial Pain Syndrome (MPS), characterized by chronic pain from myofascial trigger points (MTrPs), is frequently observed following ischemic stroke. MTrPs produce localized tenderness, referred pain, muscle weakness, restricted mobility, and autonomic symptoms, arising from muscle imbalance, spasticity, immobility, oxidative stress, and impaired muscle metabolism. Coenzyme Q10 (CoQ10), or ubiquinone, is a lipid-soluble molecule integral to mitochondrial bioenergetics, playing critical roles in ATP synthesis and antioxidative defense by neutralizing reactive oxygen species (ROS). Emerging studies link reduced CoQ10 levels to diseases involving oxidative stress, mitochondrial dysfunction, and impaired cellular energy metabolism, including ischemic stroke and musculoskeletal disorders. Clinically, stroke patients exhibit significantly decreased serum CoQ10 concentrations associated with greater stroke severity and poorer outcomes. CoQ10 deficiency potentially contributes directly to MPS by compromising mitochondrial function, increasing oxidative stress, and promoting inflammation within muscle tissues, leading to trigger point formation and chronic pain. Clinical evidence supports CoQ10 supplementation as beneficial in reducing pain intensity and improving muscle function and quality of life in patients with chronic musculoskeletal disorders. Identifying and correcting CoQ10 deficiency post-stroke may thus offer therapeutic potential to prevent or reduce MPS. Further randomized clinical trials are necessary to confirm the efficacy, optimal dosage, and long-term benefits of CoQ10 supplementation for stroke rehabilitation.

Keywords: coenzyme Q10; ischemic stroke; myofascial pain syndrome; oxidative stress.

INTRODUCTION

Stroke remains a significant global health concern, recognized as one of the leading causes of long-term disability worldwide. Approximately 85% of all stroke cases are ischemic, occurring due to thrombotic or embolic occlusion of cerebral arteries, resulting in disrupted cerebral blood flow and neuronal injury [1,2]. Among numerous complications of post-ischemic stroke, musculoskeletal issues are highly prevalent and greatly impair patient quality of life, independence, and rehabilitation outcomes [3].

Myofascial Pain Syndrome (MPS) is a common musculoskeletal complication observed following stroke, characterized by persistent pain resulting from hyperirritable nodules termed myofascial trigger points (MTrPs) within taut bands of skeletal muscle or associated fascia. These trigger points often manifest with localized tenderness, referred pain patterns, muscle dysfunction, and autonomic disturbances, significantly affecting daily functioning and overall recovery [4,5].

The underlying pathophysiology of MPS in stroke patients involves complex interactions between muscular imbalance, sustained muscle contraction, spasticity, immobility, oxidative stress, and compromised muscle metabolism [6].

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a vitamin-like, lipid-soluble antioxidant molecule integral to mitochondrial bioenergetics. It plays a pivotal role in mitochondrial electron transport and ATP production, as well as in reducing oxidative stress by scavenging reactive oxygen species (ROS) [7,8]. Recent studies suggest a significant association between CoQ10 deficiency and conditions characterized by increased oxidative stress, mitochondrial dysfunction, and impaired cellular energy metabolism, such as ischemic stroke and chronic musculoskeletal pain syndromes, including MPS [9,10].

The purpose of this literature review is to explore the potential role of Coenzyme Q10 as a risk factor contributing to the occurrence of Myofascial Pain Syndrome in patients following ischemic stroke, with emphasis on its pathophysiological mechanisms and clinical relevance.

Overview Of Ischemic Stroke

Stroke is defined by the World Health Organization (WHO) as a clinical syndrome characterized by rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular origin. Stroke is broadly classified into two categories: ischemic stroke, resulting from blockage of blood vessels, and hemorrhagic stroke, resulting from bleeding due to vessel rupture. Approximately 85% of all strokes are ischemic in nature, arising from thrombotic or embolic occlusion of the cerebral arteries [11,12].

Globally, stroke is the second leading cause of death and a major contributor to disability. In 2019, approximately 12.2 million new stroke cases and 101 million prevalent stroke cases were recorded globally, with ischemic strokes constituting the vast majority of these cases [13]. In Indonesia, stroke incidence continues to increase due to lifestyle changes, urbanization, and demographic shifts. According to data from the Indonesian Basic Health Research (Riset Kesehatan Dasar), stroke prevalence increased from 7 per mil in 2013 to 10.9 per mil population in 2018, highlighting the burden of stroke as a significant public health challenge [14]. Ischemic stroke has numerous established risk factors. Age is a strong, non-modifiable risk factor, with incidence doubling for each decade after 55 years of age. Other significant modifiable risk factors include hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, a sedentary lifestyle, and cardiovascular diseases such as atrial fibrillation [15,16]. These risk factors contribute to arterial endothelial dysfunction, accelerated atherosclerosis, and increased susceptibility to thrombosis and subsequent ischemic events.

The pathophysiology of ischemic stroke involves complex mechanisms, primarily triggered by reduced cerebral blood flow and oxygen supply to brain tissue. Key pathological events include excitotoxicity, oxidative stress, inflammation, blood-brain barrier disruption, and neuronal apoptosis. Oxidative stress, arising from the excessive production of reactive oxygen species (ROS), results in lipid peroxidation, protein oxidation, and DNA damage, exacerbating neuronal injury. Additionally, inflammation mediated by activated microglia, astrocytes, and infiltrating leukocytes releases pro-inflammatory cytokines, further perpetuating neuronal cell death through apoptosis pathways [17,18].

Musculoskeletal complications are common sequelae following ischemic stroke and significantly impede functional recovery. Among these, Myofascial Pain Syndrome (MPS) frequently emerges, characterized by chronic musculoskeletal pain due to hyperirritable spots termed myofascial trigger points (MTrPs) in muscles or fascia. MPS following stroke may develop due to prolonged immobility, abnormal muscle tone, spasticity, and compromised muscle energy metabolism, resulting in muscle ischemia, inflammation, and the formation of trigger points. This condition can severely restrict patient mobility, hinder rehabilitation progress, and diminish overall quality of life [19,20].

Myofascial Pain Syndrome (MPS)

Myofascial Pain Syndrome (MPS) is defined as a chronic musculoskeletal pain disorder characterized by the presence of myofascial trigger points (MTrPs), which are localized hyperirritable spots within taut bands of skeletal muscles or fascia. These trigger points produce pain upon palpation and can cause characteristic patterns of referred pain, limited range of motion, muscle weakness, and autonomic symptoms such as sweating or vasoconstriction [21,22].

The global prevalence of MPS varies considerably depending on the population studied, diagnostic criteria used, and specific clinical settings. However, it is estimated that approximately 30–85% of individuals experiencing chronic musculoskeletal pain have an underlying component of MPS [23]. Among ischemic stroke patients, the prevalence of MPS is notably high, often associated with chronic pain syndromes, especially shoulder pain, which affects around 30–65% of stroke survivors. The persistent presence of MPS can significantly hamper rehabilitation efforts, functional recovery, and overall patient well-being post-stroke [24,25].

Several risk factors contribute to the development of MPS among ischemic stroke survivors. Key contributors include prolonged immobility, spasticity, altered posture, and musculoskeletal dysfunctions resulting from neurological deficits. These factors collectively predispose muscles to ischemia, metabolic disturbances, and subsequent formation of trigger points. Additionally, inadequate rehabilitation, depression, and poor nutrition may exacerbate the severity and chronicity of MPS in post-stroke patients [26,27].

The pathophysiology of MPS is complex, involving an interplay of neuromuscular dysfunction, metabolic disturbances, inflammation, and oxidative stress. A widely accepted hypothesis suggests that sustained muscle contraction and ischemia lead to a local energy crisis within muscle fibers. This energy crisis impairs mitochondrial function, reduces ATP production, and contributes to anaerobic metabolism, thus increasing lactate accumulation and lowering the local pH, perpetuating muscle pain and dysfunction. Furthermore, persistent ischemia triggers inflammatory responses and the release of cytokines and reactive oxygen species (ROS), further damaging muscle tissues and perpetuating trigger point formation [28,29].

Clinically, the presence of MPS post-stroke profoundly affects patients' quality of life, hindering daily activities, reducing functional independence, and significantly limiting participation in rehabilitation programs. Chronic pain associated with MPS frequently leads to psychological distress, sleep disturbances, anxiety, and depression, exacerbating the patient's overall disability and diminishing long-term recovery outcomes [30,31].

Coenzyme Q10 (CoQ10)

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a naturally occurring lipid-soluble molecule characterized by a quinone ring with a polyisoprenoid side chain. Structurally, CoQ10 comprises a benzoquinone ring bound to a polyisoprenoid tail consisting of ten isoprene units. This hydrophobic side-chain enables CoQ10 to anchor effectively within cellular membranes, particularly in the mitochondrial inner membrane, where it exerts its primary biological functions [32,33].

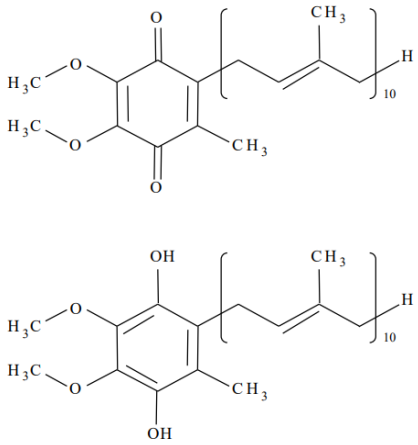

FIGURE 1: Chemical structure of the benzoquinone head and hydrophobic polyisoprene tail in reduced (Ubiquinol, bottom image), and oxidized (Rauchová, 2021).

In humans, CoQ10 is synthesized endogenously through the mevalonate pathway, involving multiple enzymatic reactions with acetyl-CoA as the initial substrate. The biosynthesis process predominantly occurs in mitochondria, endoplasmic reticulum, and Golgi apparatus. Although the liver is considered the major site of biosynthesis, CoQ10 is broadly distributed throughout tissues, with high concentrations found in organs with high metabolic rates, such as the heart, kidneys, skeletal muscles, and brain [34,35].

Coenzyme Q10 plays a critical role in cellular metabolism, primarily as an essential electron transporter in mitochondrial oxidative phosphorylation. It facilitates electron transfer from complexes I and II to complex III within the electron transport chain, thereby enabling effective ATP production. Additionally, CoQ10 exhibits potent antioxidant properties, neutralizing reactive oxygen species (ROS) and protecting cell membranes, mitochondrial DNA, proteins, and lipids from oxidative damage. This dual function underscores its importance in cellular bioenergetics and antioxidative defense mechanisms [36,37].

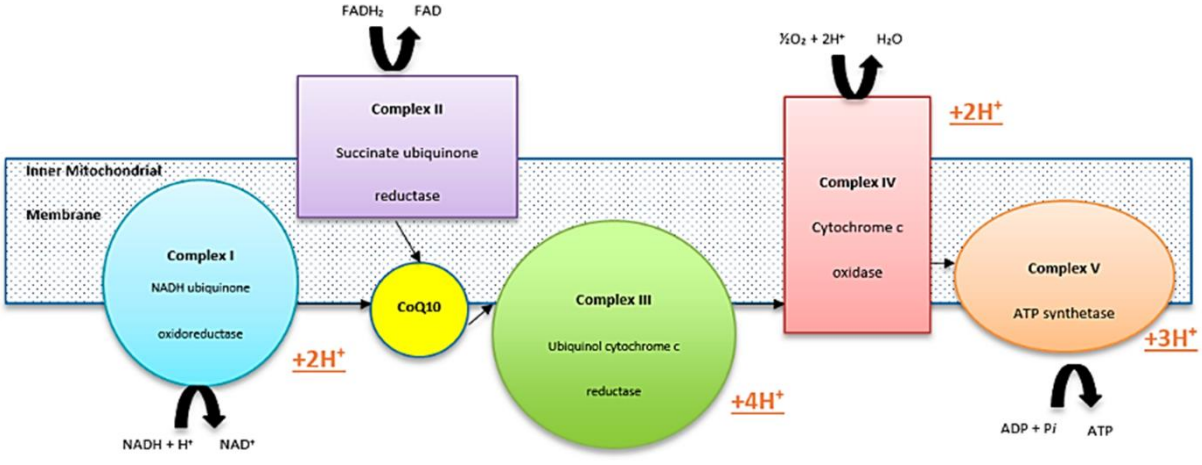

FIGURE 2: Mitochondrial electron transport chain (Manzar et al., 2020).

Physiological CoQ10 levels are known to decline progressively with aging. Moreover, certain medications, including statins (HMG-CoA reductase inhibitors), beta-blockers, and some antidepressants, have been associated with reduced endogenous CoQ10 synthesis, contributing to clinical deficiency. Pathological conditions characterized by mitochondrial dysfunction, chronic inflammation, or enhanced oxidative stress such as cardiovascular diseases, neurodegenerative disorders, and metabolic syndromes have also been linked to decreased CoQ10 levels, potentially exacerbating disease progression [38,39].

Growing evidence indicates a significant relationship between CoQ10 deficiency, oxidative stress, and inflammatory responses across various disease states. Reduced CoQ10 levels impair mitochondrial efficiency, resulting in increased ROS production, oxidative damage, and activation of inflammatory pathways. This oxidative-inflammatory axis has been implicated in numerous pathological conditions, including ischemic stroke, cardiovascular diseases, chronic musculoskeletal pain, and neurodegenerative disorders, suggesting the potential therapeutic benefit of CoQ10 supplementation in mitigating these processes [40–42].

Relationship Of Coenzyme Q10 With Ischemic Stroke And Myofascial Pain Syndrome (MPS)

Coenzyme Q10 (CoQ10) has shown significant potential as a neuroprotective agent in the context of ischemic stroke, primarily through its role as a potent antioxidant and modulator of inflammatory processes. During ischemic events, excessive reactive oxygen species (ROS) are generated, leading to oxidative stress, neuronal cell damage, and activation of inflammatory pathways. CoQ10 mitigates these harmful effects by neutralizing ROS, stabilizing mitochondrial membranes, and reducing the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α), thereby attenuating subsequent neuronal apoptosis and neurological deficits [43,44].

Several studies have investigated CoQ10 levels in patients following ischemic stroke, consistently demonstrating reduced serum CoQ10 concentrations compared to healthy controls. These decreased levels correlate significantly with stroke severity, infarct size, and poorer clinical outcomes, suggesting that CoQ10 depletion may play a critical role in stroke pathophysiology and prognosis [45,46].

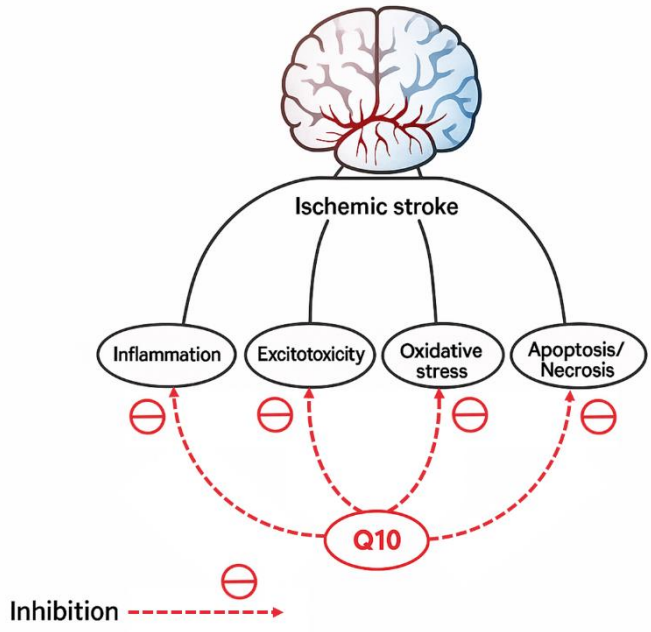

FIGURE 3: Neuroprotective effects of CoQ10 in ischemic stroke (Rodrigo et al., 2013).

The role of CoQ10 deficiency in the formation of myofascial trigger points (MTrPs) and the subsequent development of Myofascial Pain Syndrome (MPS) post-stroke has been highlighted by emerging evidence. Muscle tissues exhibiting CoQ10 deficiency suffer from compromised mitochondrial bioenergetics, increased oxidative stress, and persistent inflammatory responses, all contributing to chronic muscle pain, dysfunction, and the eventual development of trigger points. These processes perpetuate a localized energy crisis within affected muscles, thus exacerbating pain and disability commonly observed in stroke survivors [47,48].

Recent clinical studies have directly linked lower CoQ10 levels to a higher incidence of chronic musculoskeletal pain syndromes, including MPS. Silva et al. reported a significant association between CoQ10 deficiency and chronic musculoskeletal pain, indicating that inadequate cellular energy production and heightened oxidative stress in muscle tissues play crucial roles in the development and persistence of MPS [49]. Similarly, supplementation trials have shown notable improvements in pain intensity, muscle tenderness, and quality of life among patients with chronic musculoskeletal disorders receiving CoQ10 treatment, underscoring its therapeutic potential [50].

Clinically, recognizing CoQ10 deficiency in ischemic stroke patients may hold significant implications for managing post-stroke musculoskeletal complications such as MPS. Supplementation of CoQ10 could potentially reduce oxidative stress, improve mitochondrial energy metabolism, alleviate inflammation, and thereby prevent or mitigate MPS development. Thus, therapeutic administration of CoQ10 represents a promising adjunctive strategy in the holistic rehabilitation of ischemic stroke patients, warranting further research to define optimal dosage and long-term benefits [51,52].

CONCLUSION

Coenzyme Q10 (CoQ10) deficiency has emerged as a potential risk factor contributing significantly to the development of Myofascial Pain Syndrome (MPS) in patients following ischemic stroke. The depletion of CoQ10 exacerbates oxidative stress, mitochondrial dysfunction, and inflammatory processes, all of which are pivotal mechanisms implicated in both ischemic stroke and MPS pathogenesis. This biochemical imbalance promotes the formation of myofascial trigger points (MTrPs), resulting in chronic musculoskeletal pain, functional impairment, and diminished quality of life among stroke survivors.

Clinically, recognition of reduced CoQ10 levels in post-stroke patients emphasizes the importance of evaluating and potentially supplementing CoQ10 as part of comprehensive stroke rehabilitation programs. CoQ10 supplementation might mitigate oxidative stress, improve mitochondrial function, and reduce inflammation, thereby decreasing the incidence or severity of MPS post-stroke. Further research through well-designed clinical trials is necessary to clarify optimal dosage, treatment duration, and precise mechanisms by which CoQ10 supplementation influences MPS development. Such studies are essential to strengthen current evidence and establish CoQ10 as a validated therapeutic option in managing chronic musculoskeletal pain in ischemic stroke populations.

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